

## DECLARATION

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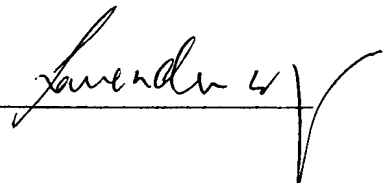
do solemnly and sincerely declare:

1. that I am well acquainted with both the English and Chinese languages, and

2. that the attached document is a true and correct translation of the application filed as PCT/CN2003/000923 filed on October 30, 2003,

and I make this declaration conscientiously believing the statement contained herein to be true in every particular.

Date April 15<sup>th</sup> 2005

Signature 

Name typed Lavender Sze

## DESCRIPTION

A rabbit skin containing biologically active substances and its use

### FIELD OF THE INVENTION

The present invention relates to a rabbit skin containing biologically active substances  
5 and its use.

### BACKGROUND OF THE INVENTION

It was reported that the extracts from inflammatory rabbit skin tissues vaccinated with  
vaccinia virus can be used for the treatment of allergic disease and have the analgesic effect.  
There has not been any method to prepare rabbit skin that contains strongly active and high  
10 yield biologically active substances.

### DETAILED DESCRIPTION OF THE INVENTION

#### Aims

The objective of the present invention is to provide a rabbit skin which is rich in  
biologically highly active substances that can be used for preparing drugs and health foods.

#### 15 Project

As a result of many years of hard work, the inventors of the present invention have  
reached this aim.

The rabbit skin of the present invention is obtained by the process including vaccinating  
rabbit (*Oryctolagus cuniculus*) skin tissues with vaccinia virus, feeding rabbit vaccinated with  
20 vaccinia virus, killing the rabbit when its skin tissues is inflamed enough, and peeling the  
rabbit.

Vaccinia virus has been used widely since the 20th century. All kinds of vaccinia virus can be used to prepare the rabbit skin of the present invention, such as Lister strain, Ikeda strain, Dairen strain, EM-63 strain, Temple of Heaven strain, LMC strain, Tashkent strain, Williamsport strain, and New York City Board of Health strain. The preferred strains are  
5 Lister strain, Ikeda strain, Dairen strain, EM-63 strain, the most preferred strain is Lister strain. All these vaccinia virus strains can be purchased from the market. The vaccinia virus strains used in the present invention can be purchased strain or strain obtained from subculture with rabbit.

The preferred vaccination method is subcutaneous vaccination, the said vaccinating rabbit  
10 skin tissues with vaccinia virus is effected by injecting subcutaneously 0.1~0.4 ml solution containing  $10^6 \sim 10^9$  viruses/ml each site, 100 to 250 sites per rabbit weighing 1.5~3 Kg.

The rabbit used in preparing the rabbit skin of present invention can be all kinds of rabbits, such as Japanese white rabbit, New Zealand white rabbit, Chinese rabbit, Blue-violet rabbit, Silver Fox rabbit, Viennese rabbit, Long hair rabbit, Himalayan albino rabbit, Pex, Belgian  
15 Hare rabbit, Lop, California rabbit, Chekered Giant, Denmark white rabbit, West Germany long hair rabbit, the preferred rabbits are Japanese white rabbit, New Zealand white Rabbit, Chinese rabbit, Blue-violet rabbit, the most preferred rabbit is Japanese white rabbit.

The said killing the rabbit when its skin tissues is inflamed enough is effected when the rabbit skin inflammatory tissue shows visible blains accompanying with changing colour  
20 from redness to mauveness and becomes thick, and its subcuticle and hip become swollen. The preferred method to kill rabbit is cervical vertebrae dislocation.

#### Effect

The rabbit skin of the present invention possesses 0.5 iu/g SART activity or more, and which also possesses the kallikrein-protease inhibition activity.

25 By extracting with organic solvent, processing with acid, processing with alkali, absorbing,

eluting and concentrating, biologically active preparations being rich in amino acids and nucleic acids can be prepared from the rabbit skin. The said amino acids include glutamic acid, glycine, alanine, valine, isoleucine, leucine, tyrosine, phenylalanine, lysine, histidine, aspartic acid, threonine and serine. The said nucleic acids include urocanic acid, uracil, hypoxanthine, xanthine and thymine.

Drug can be prepared by combining the biologically active preparations of the present invention with pharmaceutical acceptable adjuvants. This drug can be various form of preparations used clinically, including injection and tablet, the preferred form is the injection. For injections, the adjuvants can be for example injectable distilled water, normal saline, injectable vegetable oil, glucose injection, propylene glycol, polyethylene glycol, or it may be all kinds of stabilizers and emulsifiers. For tablets, capsules and granules, the adjuvants can be excipients such as starch, lactose, mannitol; binders such as crystalline cellulose, arabic gum, corn starch, gluten, polyethylene, polyvinyl alcohol, polyvinyl-pyrrolidone; disintegrants such as carboxyl methyl cellulose, poly-ethylene glycol, potato starch; lubricants such as talcum powder, magnesium stearic acid; moistening agents such as glycerol. For ointments, the adjuvants can be fat oil, paraffin, wool fat, vaseline, glycol, glycerol.

The pharmacological and clinic experiments showed that the drugs prepared from the rabbit skin of the present invention have analgesic effect against all kinds of symptomatic neuralgia, lambago, cholecystagia, angina, arterial embolism pains, acute pains from wound, burn and scald, pains in surgery or post-surgery, peptic ulcer pain, dysmenorrhea, labor pains posterior to childbirth, headache, pains induced by various tumor and so on.

The study showed that the drugs prepared from the rabbit skin of the present invention can effectively promote activation of macrophage, significantly inhibit 48-hour homologous PCA reaction induced by antibody of IgE in the model of type I allergic reaction in mice, inhibit

the activity of anti-complement in type II allergic reaction. The effects have linear correlation with the doses. So the drugs have effects on inhibiting inflammatory reaction correlated with immunity and improving immunity function.

Moreover, the drugs prepared from the rabbit skin of the present invention have  
5 anti-allergic, anti-ulcer and sedative effects and so on.

After a continuous 28-day intraperitoneally administration of the drugs prepared from the rabbit skin of the present invention in rats, no rats died and no changes induced by the drugs existed in examinations of urine, eye, blood biochemistry, pathology and anatomy. Therefore, the analgesic drugs of the present invention have little toxic effects.

10 Health food can be prepared by combining the biologically active preparations of the present invention with edible additives and nutritious substances, the said edible additives and nutritious substances include all kinds of vitamins and flavoring agents and so on. These kinds of health food have effects on improving immunity, alleviating pains, anti-allergy and anti-stress and so on.

15 The method of determination of SART (Specific Alteration of Rhythm in Environmental Temperature) activity is well known in the art (Folia pharmacol. japon. 71:211~220, 1975).

The kallikrein-protease inhibition activity referred in this description is determined as follows:

The rabbit skin was cut in pieces of 1 cm<sup>2</sup>, 4 times (w/w) of 3% phenol aqueous solution  
20 was added, then placed the mixture at 4°C for 72h, centrifuged after liquid changed into emulsion. The supernatant was filtrated to collect brown solution A. The brown solution A was boiled for 40 min in a water bath after pH was adjusted to 5.0 by 1M HCl, cooled to 28 °C promptly, centrifuged and filtrated to collect solution B. The solution B was boiled for 40 min in a water bath after pH of filtrate was adjusted to 9.2 by 1M NaOH, cooled to 28°C  
25 promptly, and filtrated to collect solution C. pH of the solution C was adjusted to 4.5 by 1M

HCl, activated charcoal was added at 30°C, stirred continuously for 4h, stopped stirring, left it for 30min, removed the supernatant, filtrated under nitrogen atmosphere. Then the activated charcoal was dipped in injectable water and washed, filtrated and discarded filtrate to collect the activated charcoal, reserved the activated charcoal. The activated charcoal was then put into injectable water, adjusted pH to 11.0 by 1M NaOH, stirred continuously for 4h, filtrated with a 0.45-µm Millipore filter under nitrogen atmosphere, washed the activated charcoal by injectable water to collect solution D. After pH of the solution D was adjusted to 6.0 by 1M HCl, the vessel was sealed, heated up and kept the temperature at 121°C for 20min, and then cooled down to under 40°C to collect solution E. The solution E was placed into a decompression distillator, replaced the air with nitrogen in the decompression distillator, distilled at 60°C under decompression, filtrated to collect solution containing biologically active substances, whose SART activity was determined. The SART activity of the solution was adjusted to 1.2iu/ml by evaporating, concentrating and diluting with distilled water. 10ml of this solution was desalted at 10 µs/cm of final conductance, dried under decompression condition, into which 1.5 ml of 0.25 M NaCl solution was added to obtain test solution. 0.2 ml of 0.25M NaCl solution was regarded as the control solution and treated with parallel process with the 0.2 ml test solution. 0.5 ml human plasma were added respectively to both solutions, placed at freezing point for 5 min, added 0.25 ml of suspension of argilla, placed at freezing point for 20 min, and filtrated. 0.1 ml of filtrate was mixed with 0.2 ml of 0.1 M Tris-HCl buffer and 0.1 ml of basic solution. Effected reaction for 20 min at 30°C, and stopped the reaction by adding 0.8 ml of 1% citric acid. The absorbance A of test solution was determined in 405 nm as the absorbance of control solution was initialized as 0.4. If A was less than 0.4, the rabbit skin from which the test solution was prepared was regarded as possessing the kallikrein-protease inhibition activity.

## EXAMPLES

The present invention will be illustrated with following non-limited examples.

### Example 1

#### Preparation of rabbit skin

5        The dry variola vaccine of vaccinia virus Lister strain was dissolved by PBS(-) (NaCl 80 g, KCl 2 g,  $\text{NaH}_2\text{PO}_4$  11.5 g,  $\text{KH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$  2 g, adding injectable  $\text{H}_2\text{O}$  to 10 L) and well shaken. 0.4 ml of this solution was injected in central inner lamina of testicle of Japanese white rabbit. Dislocating its cervical vertebra on the fourth day. Cut the scrotum, removed connective tissue in the testicle. The testicle was placed in vessel full of ice, preserved at -80  
10    °C refrigerator. The testicle was taken from refrigerator, softened for 1 h, grinded at 4°C, mixed in 1:1 with EAGLES' cultural medium (Eagle's powder 9.4 g, 10%  $\text{NaHCO}_3$  12.5~22.0 ml, glutamine 10 ml, injectable  $\text{H}_2\text{O}$  1 L), packed, frozen at -80°C in refrigerator for 1 h, thawed at 37°C in water bath, centrifuged with 3500 rpm at 4°C for 20 min, packed by 10 ml. The subculture antigen was preserved at -80°C in refrigerator.

15        The virus solution of subculture antigen was taken from the -80°C refrigerator, thawed at 30°C in incubator. 5 ml of the virus solution was added into 500 ml of PBS(-) by a 10-ml syringe, well shaken and diluted to injection of  $10^9$  virus/ml. A Japanese white rabbit weighing 3 kg with its back shaved, was sterilized with 75% ethanol, injected subcutaneously with the virus injection 0.4 ml per site in 200 sites with no leaking, no injecting without the  
20    virus injection and no puncturing throughout the skin. The rabbit injected was fed for 4 days. When inflammatory tissue showed that skin surface had visible blains accompanying with changing colour from redness to mauveness and skin became thick, and subcuticle and hip became swollen, killed the rabbit by cervical vertebra dislocation and peeled in 15 min. The skin of rabbit was packed in plastic bag, preserved at -18°C in refrigerator prior to use. The

rabbit skin weighed 349 g, its SART activity was 0.85 iu/g, and its absorbance was 0.07. The results indicated that it possessed the kallikrein-protease inhibition activity.

#### Example 2

##### Preparation of rabbit skin

5 The vaccinia virus Ikeda strain and New Zealand white rabbit were used to prepare the subculture antigen according to example 1.

The virus solution of subculture antigen was taken from the -80°C refrigerator, thawed at 30°C in incubator. 5 ml of the virus solution was added into 500 ml of PBS(-) by a 10-ml syringe, well shaken and diluted to injection of  $10^9$  virus/ml. A New Zealand white rabbit  
10 weighing 2.75 kg with its back shaved, was sterilized with 75% ethanol, injected subcutaneously with the virus injection 0.3 ml per site in 250 sites with no leaking, no injecting without the virus injection and no puncturing throughout skin. The rabbit injected was fed for 3 days. When inflammatory tissue showed that skin surface had visible blains accompanying with changing colour from redness to mauveness and skin became thick, and  
15 subcuticle and hip became swollen, killed the rabbit by cervical vertebra dislocation and peeled in 15 min. The skin of rabbit was packed in plastic bag, preserved at -18°C in refrigerator prior to use. The skin of rabbit weighed 302 g, its SART activity was 0.60 iu/g, and its absorbance was 0.1. The results indicated that it possessed the kallikrein-protease inhibition activity.

#### 20 Example 3

##### Preparation of rabbit skin

The vaccinia virus Dairen strain and Chinese rabbit were used to prepare the subculture antigen according to example 1.

The virus solution of subculture antigen was taken from the -80°C refrigerator, thawed at  
25 30°C in incubator. 5 ml of the virus solution was added into 500 ml of PBS(-) by a 10-ml



syringe, well shaken and diluted to injection of  $10^6$  virus/ml. A Chinese rabbit weighing 1.5 kg with its back shaved, was sterilized with 75 % ethanol, injected subcutaneously with the virus injection 0.1 ml per site in 250 sites with no leaking, no injecting without the virus injection and no puncturing throughout skin. The rabbit injected was fed for 3 days. When inflammatory tissue showed that skin surface had visible blains accompanying with changing colour from redness to mauveness and skin became thick, and subcuticle and hip became swollen, killed the rabbit by cervical vertebra dislocation and peeled in 15 min. The skin of rabbit was packed in plastic bag, preserved at  $-18^{\circ}\text{C}$  in refrigerator prior to use. The skin of rabbit weighed 176 g, its SART activity was 0.50 iu/g, and its absorbance was 0.15. The results indicated that it possessed the kallikrein-protease inhibition activity.

#### Example 4

##### Preparation of rabbit skin

The vaccinia virus EM-63 strain and Blue-violet rabbit were used to prepare the subculture antigen according to example 1.

The virus solution of subculture antigen was taken from the  $-80^{\circ}\text{C}$  refrigerator, thawed at  $30^{\circ}\text{C}$  in incubator. 5 ml of the virus solution was added into 500 ml of PBS(-) by a 10-ml syringe, well shaken and diluted to injection of  $10^7$  virus/ml. A Blue-violet rabbit weighing 2 kg with its back shaved, was sterilized with 75% ethanol, injected subcutaneously with the virus injection 0.2 ml per site in 100 sites with no leaking, no injecting without the virus injection and no puncturing throughout skin. The rabbit injected was fed for 3 days. When inflammatory tissue showed that skin surface had visible blains accompanying with changing colour from redness to mauveness and skin became thick, and subcuticle and hip became swollen, killed the rabbit by cervical vertebra dislocation and peeled in 15 min. The skin of rabbit was packed in plastic bag, preserved at  $-18^{\circ}\text{C}$  in refrigerator prior to use. The skin of rabbit weighed 230 g, its SART activity was 0.55 iu/g, and its absorbance was 0.12. The

results indicated that it possessed the kallikrein-protease inhibition activity.

#### Example 5

##### Preparation of rabbit skin

The vaccinia virus Lister strain and New Zealand white rabbit were used to prepare the  
5 subculture antigen according to example 1.

The virus solution of subculture antigen was taken from the -80°C refrigerator, thawed at  
30°C in incubator. 5 ml of the virus solution was added into 500 ml of PBS(-) by a 10-ml  
syringe, well shaken and diluted to injection of  $10^9$  virus/ml. A New Zealand white rabbit  
weighing 2.75 kg with its back shaved, was sterilized with 75% ethanol, injected  
10 subcutaneously with the virus injection 0.3 ml per site in 200 sites with no leaking, no  
injecting without the virus injection and no puncturing throughout skin. The rabbit injected  
was fed for 3 days. When inflammatory tissue showed that skin surface had visible blains  
accompanying with changing colour from redness to mauveness and skin became thick, and  
subcuticle and hip became swollen, the rabbit was killed by cervical vertebra dislocation and  
15 peeled in 15 min. The skin of rabbit was packed in plastic bag, preserved at -18°C in  
refrigerator prior to use. The skin of rabbit weighed 310 g, its SART activity was 0.79 iu/g,  
and its absorbance was 0.09. The results indicated that it possessed the kallikrein-protease  
inhibition activity.

#### Example 6

##### Preparation of rabbit skin

20 The vaccinia virus Lister strain and Chinese rabbit were used to prepare the subculture  
antigen according to example 1.

The virus solution of subculture antigen was taken from the -80°C refrigerator, thawed at  
30°C in incubator. 5 ml of the virus solution was added into 500 ml of PBS(-) by a 10-ml  
25 syringe, well shaken and diluted to injection of  $10^6$  virus/ml. A Chinese rabbit weighing 1.5

kg with its back shaved, was sterilized with 75% ethanol, injected subcutaneously with the virus injection 0.1 ml per site in 250 sites with no leaking, no injecting without the virus injection and no puncturing throughout skin. The rabbit injected was fed for 3 days. When inflammatory tissue showed that skin surface had visible blains accompanying with changing colour from redness to mauveness and skin became thick, and subcuticle and hip became swollen, killed the rabbit by cervical vertebra dislocation and peeled in 15 min. The skin of rabbit was packed in plastic bag, preserved at -18°C in refrigerator prior to use. The skin of rabbit weighed 185 g, its SART activity was 0.71 iu/g, and its absorbance was 0.11. The results indicated that it possessed the kallikrein-protease inhibition activity.

#### 10 Example 7

##### Preparation of rabbit skin

The vaccinia virus Lister strain and Blue-violet rabbit were used to prepare the subculture antigen according to example 1.

The virus solution of subculture antigen was taken from the -80°C refrigerator, thawed at 30°C in incubator. 5 ml of the virus solution was added into 500 ml of PBS(-) by a 10-ml syringe, well shaken and diluted to injection of  $10^7$  virus/ml. A Blue-violet rabbit weighing 2 kg with its back shaved, was sterilized with 75% ethanol, injected subcutaneously with the virus injection 0.2 ml per site in 100 sites with no leaking, no injecting without the virus injection and no puncturing throughout skin. The rabbit injected was fed for 3 days. When inflammatory tissue showed that skin surface had visible blains accompanying with changing colour from redness to mauveness and skin became thick, and subcuticle and hip became swollen, killed the rabbit by cervical vertebra dislocation and peeled in 15 min. The skin of rabbit was packed in plastic bag, preserved at -18°C in refrigerator prior to use. The skin of rabbit weighed 235 g, its SART activity was 0.74 iu/g, and its absorbance was 0.13. The results indicated that it possessed the kallikrein-protease inhibition activity.

### Example 8

#### Preparation of rabbit skin

The vaccinia virus Ikeda strain and Japanese white rabbit were used to prepare the subculture antigen according to example 1.

5      The virus solution of subculture antigen was taken from the  $-80^{\circ}\text{C}$  refrigerator, thawed at  $30^{\circ}\text{C}$  in incubator. 5 ml virus solution was added into 500 ml PBS (-) by a 10-ml syringe, well shaken and diluted to injection of  $10^9$  virus/ml. A Japanese white rabbit weighing 3 kg with its back shaved, was sterilized with 75% ethanol, injected subcutaneously with the virus injection 0.3 ml per site in 200 sites with no leaking, no injecting without the virus injection  
10      and no puncturing throughout skin. The rabbit injected was fed for 3 days. When inflammatory tissue showed that skin surface had visible blains accompanying with changing colour from redness to mauveness and skin became thick, and subcuticle and hip became swollen, the rabbit was killed by cervical vertebra dislocation and peeled in 15 min. The skin of rabbit was packed in plastic bag, preserved at  $-18^{\circ}\text{C}$  in refrigerator prior to use. The skin  
15      of rabbit weighed 335 g, its SART activity was 0.70 iu/g, and its absorbance was 0.12. The results indicated that it possessed the kallikrein-protease inhibition activity.

### Example 9

#### Preparation of rabbit skin

The vaccinia virus Dairen strain and Japanese white rabbit were used to prepare for the  
20      subculture antigen according to example 1.

The virus solution of subculture antigen was taken from the  $-80^{\circ}\text{C}$  refrigerator, thawed at  $30^{\circ}\text{C}$  in incubator. 5 ml of the virus solution was added into 500 ml of PBS (-) by a 10-ml syringe, well shaken and diluted to injection of  $10^6$  virus/ml. A Japanese white rabbit weighing 3 kg with its back shaved, was sterilized with 75 % ethanol, injected

subcutaneously with the virus injection 0.1 ml per site in 200 sites with no leaking, no injecting without the virus injection and no puncturing throughout skin. The rabbit injected was fed for 3 days. When inflammatory tissue showed that skin surface had visible blains accompanying with changing colour from redness to mauveness and skin became thick, and subcuticle and hip became swollen, killed the rabbit by cervical vertebra dislocation and peeled in 15 min. The skin of rabbit was packed in plastic bag, preserved at -18°C in refrigerator prior to use. The skin of rabbit weighed 336 g, its SART activity was 0.61 iu/g, and its absorbance was 0.14. The results indicated that it possessed the kallikrein-protease inhibition activity.

#### 10     Example 10

##### Preparation of rabbit skin

The vaccinia virus EM-63 strain and Japanese white rabbit were used to prepare the subculture antigen according to example 1.

15     The virus solution of subculture antigen was taken from the -80°C refrigerator, thawed at 30°C in incubator. 5 ml of the virus solution was added into 500 ml of PBS(-) by a 10-ml syringe, well shaken and diluted to injection of  $10^7$  virus/ml. A Japanese white rabbit weighing 3 kg with its back shaved, was sterilized with 75% ethanol, injected subcutaneously with the virus injection 0.2 ml per site in 200 sites with no leaking, no injecting without the virus injection and no puncturing throughout skin. The rabbit injected was fed for 3 days.

20     When inflammatory tissue showed that skin surface had visible blains accompanying with changing colour from redness to mauveness and skin became thick, and subcuticle and hip became swollen, killed the rabbit by cervical vertebra dislocation and peeled in 15 min. The skin of rabbit was packed in plastic bag, preserved at -18°C in refrigerator prior to use. The skin of rabbit weighed 335 g, its SART activity was 0.66 iu/g, and its absorbance was 0.12.

25     The results indicated that it possessed the kallikrein-protease inhibition activity.

### Example 11

#### Extraction of bioactive substances.

200 g each of the rabbit skins prepared according to example 1~10 were cut into pieces of 1 cm<sup>2</sup>, added into 4 times (w/w) of 3% phenol solution, placed at 4°C for 72h, centrifuged  
5 after liquid changed into emulsion. The centrifuged liquid was filtrated to collect brown solution A. After solution A's pH was adjusted to 5.0 by 1M HCl, boiled solution A in a water bath for 40 min and cooled down to 28°C immediately, centrifuged, and filtrated to collect solution B. After pH of filtrate was adjusted to 9.2 by 1M NaOH, the solution B was boiling for 40 min in a water bath, cooled down to 28°C immediately, and filtrated to collect solution  
10 C. After pH of filtrate was adjusted to 4.5 by 1M HCl, 50 g of activated charcoal was added to the solution C at 30°C, stirred continuously for 4h, stopped stirring, left it for 30min, removed the supernatant, filtrated under nitrogen atmosphere. The activated charcoal was dipped in injectable water and washed, filtrated and removed filtrate to collect and reserve the activated charcoal. The activated charcoal was then added into 400 ml injectable water in  
15 which pH was adjusted to 11.0 by 1M NaOH, stirred continuously for 4h, filtrated with a 0.45-μm Millipore filter under nitrogen atmosphere, washed by 40 ml of injectable water to collect solution D. After pH of the solution D was adjusted to 6.0 by 1M HCl, the vessel was sealed, heated up and kept the temperature at 121°C for 20min and cooled down to under 40 °C to collect solution E. The solution E in decompression distillator under nitrogen was  
20 decompressed and evaporated at 60°C till the volume was 5 ml and filtrated to collect preparation of 5 ml of solution containing bioactive substances. The content of amino acids and nucleic acids below were determined (μg/ml):

| Sample        | Exam.1 | Exam.2 | Exam.3 | Exam.4 | Exam.5 | Exam.6 | Exam.7 | Exam.8 | Exam.9 | Exam.10 |
|---------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|---------|
| Glutamic acid | 1.64   | 0.85   | 0.70   | 0.80   | 1.54   | 1.20   | 1.40   | 1.12   | 0.98   | 1.03    |
| Glycine       | 0.92   | 0.51   | 0.33   | 0.49   | 0.86   | 0.73   | 0.80   | 0.70   | 0.55   | 0.61    |
| Alanine       | 0.96   | 0.64   | 0.59   | 0.60   | 0.92   | 0.77   | 0.83   | 0.76   | 0.66   | 0.70    |
| Valine        | 0.66   | 0.34   | 0.23   | 0.29   | 0.62   | 0.57   | 0.61   | 0.51   | 0.39   | 0.45    |
| Isoleucine    | 0.42   | 0.17   | 0.10   | 0.14   | 0.40   | 0.32   | 0.38   | 0.30   | 0.26   | 0.28    |
| Leucine       | 0.67   | 0.22   | 0.11   | 0.16   | 0.66   | 0.53   | 0.60   | 0.46   | 0.35   | 0.41    |
| Tyrosine      | 0.83   | 0.30   | 0.25   | 0.20   | 0.77   | 0.61   | 0.69   | 0.52   | 0.36   | 0.44    |
| Phenylalanine | 0.55   | 0.26   | 0.24   | 0.25   | 0.53   | 0.42   | 0.48   | 0.34   | 0.30   | 0.33    |
| Lysine        | 0.47   | 0.11   | 0.09   | 0.10   | 0.45   | 0.39   | 0.34   | 0.34   | 0.19   | 0.26    |
| Histidine     | 0.64   | 0.24   | 0.18   | 0.21   | 0.57   | 0.43   | 0.53   | 0.41   | 0.31   | 0.35    |
| Aspartic acid | 0.68   | 0.44   | 0.39   | 0.40   | 0.61   | 0.57   | 0.58   | 0.49   | 0.45   | 0.46    |
| Threonine     | 0.51   | 0.24   | 0.11   | 0.16   | 0.50   | 0.42   | 0.46   | 0.38   | 0.30   | 0.34    |
| Serine        | 1.01   | 0.69   | 0.66   | 0.67   | 0.98   | 0.79   | 0.88   | 0.75   | 0.70   | 0.71    |
| Urocanic acid | 25.00  | 13.24  | 12.52  | 13.00  | 24.75  | 22.39  | 24.00  | 20.01  | 16.55  | 17.64   |
| Uracil        | 16.12  | 6.66   | 5.51   | 6.16   | 14.31  | 10.46  | 13.19  | 10.00  | 7.12   | 8.54    |
| Hypoxanthine  | 1.71   | 0.85   | 0.80   | 0.81   | 1.65   | 1.11   | 1.34   | 1.01   | 0.89   | 0.99    |
| Xanthine      | 12.44  | 6.13   | 5.21   | 5.79   | 12.00  | 9.98   | 11.67  | 9.62   | 6.39   | 8.13    |
| Thymine       | 3.38   | 1.99   | 1.15   | 1.54   | 3.30   | 2.77   | 3.19   | 2.49   | 2.04   | 2.44    |

### Example 12

#### Preparation of drug

The analgesic injection was prepared by formula below using regular method.

|   |        |
|---|--------|
| Preparation from rabbit skin according to example 2 | 5 ml   |
| NaCl  | 2.6 g  |
| Injectable distilled water                          | 300 ml |

### Example 13

#### Preparation of tablet

The analgesic tablet was prepared by formula below using regular method.

|   |        |
|---|--------|
| Preparation from rabbit skin according to example 1 | 50 ml  |
| Lactose   | 125 mg |
| Crystalline cellulose                               | 20 g   |
| Magnesium stearic acid                              | 5 mg   |

### Example 14

#### Preparation of health food

The health food was prepared by formula below using regular method.

|   |         |
|---|---------|
| Preparation from rabbit skin according to example 1 | 50 ml   |
| Sucrose   | 125 mg  |
| Citric acid   | 20 mg   |
| Vitamin C   | 5 mg    |
| Water   | 1000 ml |